Short-term effects of ocular 2% dorzolamide, 0.5% timolol or 0.005% latanoprost on the anterior segment architecture in healthy cats: a prospective study.

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Abstract

Dorzolamide 2%, timolol 0.5% and latanoprost 0.005% are widely used in the medical management of glaucoma in humans and pets. In this study, we wanted to evaluate the effect of these three molecules belonging to different hypotensive families on intraocular pressure (IOP) and anterior segment architecture in clinically healthy cats and compare these data with those obtained in a previous study under the same conditions in healthy dogs. In this prospective study 45 cats were included and divided into 3 homogeneous groups. For 7 days eye drops were instilled in the right eye (treated eye), dorzolamide 2% BID for the first group, timolol 0.5% BID for the second group and latanoprost 0.005% SID for the third group. The left (untreated) eye of all these cats constitute a control group useful for the statistical analysis of the data. On D0 and D7, the IOP was measured with Tonovet® and then, a high frequency ultrasound (ultrasound biomicroscopy UBM) was undertaken under general anesthesia. A biostatistical study of the 1440 data was then performed. Statistical test validated the use of the controlateral eye as a control, and the representativeness of a sample of 15 animals per group. At D7, the IOP of healthy cats treated with dorzolamide 2% BID decreased significantly whereas no variation was obtained with instillation of timolol 0.5% and latanoprost 0.005%. According to our protocol, these three hypotensive molecules do not significantly affect the architecture of the anterior segment of the clinically healthy feline eye as in dogs.

Keywords

Cats, dorzolamide, latanoprost, timolol, UBM.

Running title

Effects of three anti-glaucomatous drugs on the anterior segment architecture in cats.

Introduction

A common feature of all glaucoma in animals is the neurodegenerative disorder of retinal ganglion cells (RGCs) and their axons, an abnormal increase in intraocular pressure (IOP) represents a constant risk factor [Stiles, 2013]. The IOP is maintained at a relatively constant level and the rate of aqueous humor (AH) formation equals the outflow. Increase in IOP results from impairment of the aqueous humor outflow through the trabecular conventional pathway and/or through the uveoscleral pathway. It is estimated that glaucoma can affect about 1% of cats over the age of seven [Kroll et al., 2001] and most cases of feline glaucoma are secondary [Stiles, 2013].

Current therapy for feline glaucoma follows the same guidelines used in other species. Medical therapeutic option includes many topical hypotensive agents used in humans and dogs. Among hypotensive drugs, 3 families are commonly used: carbonic anhydrase inhibitors (such as dorzolamide), beta-blockers (such as timolol) and prostaglandin analogs (such as latanoprost). Dorzolamide reduces the active formation of HA by inhibiting the action of carbonic anhydrase, which is found abundantly in the ciliary body epithelial cells. Timolol as a beta-blocker, lowers aqueous humor flow by altering the adrenergic neuronal control of aqueous humor formation by blockade of the beta-receptors in the ciliary body processes, it may also inhibit active transport and ultrafiltration related to sodium transfer system. Latanoprost reduces IOP by increasing the uveoscleral outflow. The remodeling of the extracellular matrix between the ciliary muscle fibers by local metalloproteases contributes to this pharmacological effect [Plummer et al., 2013].

In a recent study by Poinsard et al., 2018, these three hypotensive drugs lowered significantly IOP in dogs without modification of the biometry of the iridocorneal angle (ICA). This result is consistent with the hypotensive effect of dorzolamide and timolol on ciliary body epithelium but it is more surprising with latanoprost which increases the uveoscleral outflow of aqueous

humor, all the more so as a previous study shows that the biometry of the anterior segment and the ciliary cleft is modified two hours after the application of a drop of latanoprost 0,005% in dogs [Gelatt and Mackay, 2001].

The goal of this study was to compare the effect of these three hypotensive molecules on IOP and biometry of the anterior segment of healthy cats, as well as to compare these data with those obtained by Poinsard et al., 2018 in healthy dogs with the same protocol under the same conditions. To evaluate the biometry of the anterior segment, we used high-frequency immersion ultrasound with high definition (20-50µm) for structures up to 5mm deep [Leibmann, 1998], while being non-invasive, and for which most of the parameters of the anterior segment have already been objectified in healthy cats [Aubin, 2003].

Materials and Methods

1. Inclusion criteria

This prospective study with a control group was performed using 45 healthy cats without any current local or systemic treatment. These 45 cats belonged to staff or customers of the Lorrainevet veterinary clinic. All the dogs were included with the consent of their owners. A complete general and ophthalmic examination including slit-lamp biomicroscopy and indirect ophthalmoscopy without pupillary dilatation was performed, followed by an evaluation of IOP using a rebound tonometer (Tonovet®, Icare, Vantaa, Finland). All animals with an ophthalmologic history or a difference greater than 2 mmHg IOP (on an average of three IOP measurements) on both eyes were excluded from the study.

Commenté [MOU1]: cats

2. Experimental protocol

Cats were divided into 3 homogeneous groups (weight, age, sex, race) of 15 cats (Table I). The study was done in two steps, spaced 7 days apart. The first step (D0) was performed in a mesopic environment, a complete general and ophthalmic examination, without dilation and without any instillation, was carried out between 10 am and 1 pm for each animal. IOP was an average of three measures on each eye. Ultrasound biomicroscopy (UBM) examination (Aviso®, Quantel Medical, Cournon d'Auvergne, France) was then performed under isoflurane gas anesthesia after medetomidine premedication and ketamine induction. At the awakening of each animal, eye drops were instilled into the right eye. For group 1, one drop of dorzolamide 2% (Trusopt 20mg / ml eye drops ND, MSD, Courbevoie, France) was instilled twice daily, at 7am and 7pm, from D0 at 7pm until D7 at 7am. For group 2, one drop of 0.5% timolol (Timoptol 0.5% eye drops, MSD, Courbevoie, France) was instilled twice daily according to the same protocol as group 1. For group 3, one drop of latanoprost 0.005% (Xalatan 0.005% eye drops ND, Pfizer, Paris, France) was instilled once a day at 10pm in the fornix of the right eye for seven days, from D0 at 10 pm until D6 at 10 pm included.

In the second step, on day 7, all animals were re-examined 12 hours after the last drop of latanoprost and 6 hours after the last drop of dorzolamide or timolol, with the same procedure under the same conditions as on D0. All examinations and UBM ultrasound were performed by the same operator on D0 and D7.

3. UBM high frequency ocular ultrasound

The ultrasound biomicroscopy for this study was a 50Mhz monotransducer with immersion probe with a geometric focalization and line scanning (UBM Aviso®, Quantel Medical, Cournon d'Auvergne, France). The patient was positioned in dorsal recumbency with its head stabilized in a vacuum pillow. Two video sequences were recorded for each eye at D0 and D7. The first sequence was recorded by placing the probe both centrally and perpendicular to the corneal surface to determine the distance between the apex of the corneal endothelium and the

apex of the anterior capsule of the lens, at the 12 o'clock position. In the second sequence, the outflow pathways were evaluated in the dorsal quadrant with the probe placed perpendicular to the corneoscleral limbus at the 12 o'clock position. From each video sequence, one image was chosen for analysis (Figure 1).

4. The anterior segment parameters

Nine parameters were evaluated (Figure 2): (a) the ICA , (b) the width of the entrance of the ciliary cleft (CC), (c) the width of the mid-CC, (d) the length of CC, (e) the depth of the anterior chamber (AC), (f) the thickness of cornea at the corneoscleral limbus note, (g) the distance between Schwalbe's line (the borderline between the cornea and sclera) and the anterior lens capsule according to Kawata and Hasegawa., 2013 and (h) the area of the ciliary cleft. These parameters were those described by Dulaurent et al., 2012 and used by Poinsard et al., 2018. The ICA (a) was the angle formed by the base of the iris in the region of the CC entry and the inner corneoscleral junction. The length of the CC noted (d) corresponded to the distance between the pectinate ligament (or the most anterior visible portion of the uveal trabecular meshwork) and the anterior part of the ciliary body. The width of the CC entry, marked (b) was the distance between the corneoscleral limbus and the iris root. The width of the mid-CC (c) was the distance between the inner sclera and the ciliary process in the central portion of the CC. The anterior chamber depth (e) was determined as the distance between the corneal endothelium in the apical region of the cornea and the anterior pole of the lens. The thickness of the cornea at the limbus (f) was the measure between the epithelium of the cornea and the endothelium in its most peripheral transparent part. The distance between the anterior capsule of the lens and the Schwalbe's line (g) was described by Kawata and Hasegawa., 2013. The area of the ciliary cleft (h) was calculated by the area formula (CC) = (d / 2 x (b + c) / 2) + ((cxd) / 4). All these measurements were performed by the UBM software caliper.

5. Statistical evaluation

For this study, 45 cats were divided into 3 homogeneous groups (weight, racial type, sex, age) of 15 individuals. Sample size n = 15 was determined using Student's t-test. Only five breeds of cats with a majority of European cats was represented in the three groups, the distribution was made in such a way as to obtain ages between 1 year and 10 years, an average weight of 4.1 kg and a male / female ratio close to 50% (Table I). Each animal was submitted to only one experiment (one type of eye drops) and two general anesthesia 7 days apart. The 1440 data obtained, including measurements of IOP and anterior segment biometry on the left (untreated) and right (treated) eyes, on D0 and D7 were integrated into a statistical model, in which the experimental unit was a cat, and the variable factor was the type of eyedrops instilled for 7 days. The objective of the statistical study was to determine the effects of these three molecules on anterior segment biometry and IOP. For this, two statistical methods were used: the non-parametric Wilcoxon test to evaluate the significant or non-significant differences between two independent groups and a one-way analysis of variance (ANOVA) to compare the sample means. The level of significance was set at $p<.05$ for all statistical analyses.

Results

The IOP and biometric measurements of the anterior segment of the untreated eye (left eye) did not significantly differ between D0 and D7. And no significant difference in the biometric data of the anterior segment was found on day 0 between the untreated eye and the treated eye. After one week of instillation of dorzolamide 2%, the IOP of the treated eye was significantly 1mmHg lower (Figure 3). This decrease was relatively moderate (5.3%). After one week of instillation of latanosprost or timolol, the IOP of the treated eye did not significantly decrease (Figure 3). About biometric data, ICA values (a), the width of the entrance of the CC (b), the width of the mid-CC (c), the length of the CC (d), the anterior chamber depth (e), the distance between the

anterior capsule of the lens and the Schwalbe's line (g) and the area of the ciliary cleft (h) were not significantly altered after 7 days of instillation whatever the eye drops. Only a significant decrease of 1.4% in corneal thickness (f) was observed with the instillation of dorzolamide (Figure 4), whereas there was a significant increase of 1.6% in thickness of the cornea (f) with the instillation of timolol (Figure 4).

Discussion

In this study, the parameters measured on the untreated eye (IOP and biometric data) did not vary between D0 and D7. It was therefore admitted that eye drops instilled on the treated eye (OD) for 7 days had no significant effect on the parameters measured on the untreated eye (OS) and this despite a possible systemic diffusion of eye drops. In addition, the absence of a significant difference in the data measured between the treated (OD) and untreated (OS) eye on D0 allowed to validate the use of the untreated eye (OS) as a control at D0 and D7. The study could also have been performed by comparing the data of the treated eye (OD) to D0 and D7. Both analyses were performed with the same statistical tests and we observed the same variations.

In contrast with healthy dogs for which these three types of hypotensive agents cause a significant decrease in IOP [Poinsard et al., 2018], only instillation of dorzolamide at 2% twice daily for 7 days resulted in a moderate but significant decrease in IOP in healthy cats in this study. This result is similar to previous studies evaluating the effects of 2% dorzolamide instilled in the eyes of healthy cats [Rainbow and Dziezyc, 2003], [Dietrich et al., 2007] and [Rankin et al., 2012]. This moderate decrease in IOP of 1 mmHg (5.5%) is close to the decrease (1.6 mmHg) in the Dietrich study (2007) when 2% dorzolamide is instilled twice daily. Increasing the frequency of instillation of dorzolamide 2% to 3 times daily does not appear to

197 significantly increase the hypotensive effect of dorzolamide in healthy cats [Dietrich et al.,
198 2007]. This modest effect of topical carbonic anhydrase inhibitors on the feline eye is also
199 viewed in an earlier study of 20 healthy cats, where IOP did not significantly decrease after
200 instillation of 1% brinzolamide for 7 days, twice a day [Gray and al., 2003]. This moderate
201 response in healthy cats does not question the interest of dorzolamide in the medical
202 management of glaucoma in cats, since the Sigle study in 2011 [Sigle and al., 2011] reveals an
203 interesting decrease in IOP of 7 cats with primary congenital glaucoma with dorzolamide
204 instilled 3 times a day.
205 The instillation twice daily of timolol for 7 days on the eyes of healthy cats did not lead to a
206 significant reduction in IOP between day 0 and day 7 in this study. This result is similar to that
207 obtained in the Kiland study [Kiland and al., 2016] and contrary to the older studies of Wilkie
208 and Latimer in 1991 and Colasanti and Trotter in 1981. In the Dietrich study (2007),
209 concomitant administration of dorzolamide and timolol did not have a more intense hypotensive
210 effect than dorzolamide alone.
211 Finally, instillation of latanoprost once daily for 7 days in healthy cats' eyes did not decrease
212 the IOP between day 0 and day 7 in this study, which is consistent with previous studies on the
213 effects of latanoprost on the IOP of healthy cats [Mc Donald and al., 2016], [Studer and al.,
214 2000]. This lack of efficacy of PGF2 alpha receptor analogs is attributed to species differences
215 in prostaglandin receptors in the ciliary bodies of the cat's eye that express EP and DP receptors
216 rather than FP receptors, found in particular in humans [Regnier and al., 2006].
217 The absence of significant modification of the anterior segment biometry in this study during
218 instillation of timolol and latanoprost in healthy cats confirms the lack of response of these
219 molecules to IOP after 7 days of treatment.
220 Regarding dorzolamide 2%, the absence of significant modification on the biometry of the
221 anterior segment confirms that dorzolamide acts on the IOP by lowering the production of HA

without interacting on the outflow pathway of HA. The lack of effect on AIC biometrics of these three molecules in healthy cats is similar to the results obtained in healthy dogs using the same protocol and the same operator [Poinsard and al., 2018]. A decrease of 1.4% in the thickness of the peripheral cornea in cats treated with dorzolamide was found, this decrease similar to treated dogs [Poinsard and al., 2018] can be related to a transient dehydration of the cornea. Conversely, a 1.6% increase in the thickness of the peripheral cornea in cats treated with timolol was noted: this can be related to a transient edema of the cornea.

Differences in IOP results with some studies during instillation of timolol may be related to the type of tonometer used. Nevertheless, Tonovet® provides accurate and reproducible IOP measurements in cats [McLellan and al., 2013]. Although all the qualitative measurements on the anterior chamber angle and sclerociliary cleft are perfectly described by Dulaurent et al., 2012, the precision of the UBM measurements remains a variable dependent on the experience of the operator. It is important to remember that the comparison of the data between healthy dogs and healthy cats is reinforced by the fact that these two studies were carried out by the same operator and under the same conditions.

This study has the same limitations as the study by Poinsard et al., 2018, limitations related to the recruitment mode (private structure) causing a double selection bias, especially for breeds that may have specificities, and the number of cats presented. Even if these three molecules showed little or no influence on IOP and anterior segment biometry in healthy cats, it would be interesting to carry out the same study in a context of glaucomatous cats.

Conclusion

This prospective study revealed a significant decrease in IOP in healthy cats treated with dorzolamide at 2% BID for 7 days. Timolol 1% BID and latanoprost SID have no effect on IOP after 7 days of treatment in healthy cats. Finally, dorzolamide 2%, timolol 0.5% and latanoprost

0.005% have no effect on the biometry of AIC in healthy cats with the protocol used and the duration studied.

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Conflict of interest:

The Author(s) declare(s) that there is no conflict of interest.

References:

- Aubin, M.L., Powell, C.C., Gionfriddo, J.R. and Fails, A.D. 2003. Ultrasound biomicroscopy of the feline anterior segment. Vet. Ophthalmo. 6, 15-17.

- Colasanti, B.K. and Trotter, R.R. 1981. Effects of selective beta 1- and beta 2- adrenoreceptor agonists and antagonist on intraocular pressure in the cat Invest Ophthalmol Vis Sci. 20, 69-76.

- Dietrich, U.M., Chandler, M.J., Cooper, T., Vidyashankar, A. and Chen, G. 2007. Effect of topical 2% dorzolamide hydrochloride alone and in combination with 0,5% timolol maleate on intraocular pressure in normal feline eyes. Vet Ophthalmo. 10, 95-100.

- Dulaurent, T., Goulle, F., Dulaurent, A., Mentek, M., Peiffer, R.L. and Isard PF. 2012. Effect of mydriasis induced by topical instillations of 0.5% tropicamide on the anterior segment in normotensive dogs using ultrasound biomicroscopy. Vet. Ophthalmol. 15, 8-13.

- Gelatt, K.N. and MacKay, E.O. 2001. Effects of different dose schedules of latanoprost on intraocular pressure and pupil size in the glaucomatous Beagle. Vet. Ophthalmo. 4, 283-288.

- Gray, H.E., Willis, A.M. and Morgan, R.V. 2003. Effects of topical administration of 1% brinzolamide on normal cat eyes. Vet. Ophthalmo. 6, 285-290.

- Kawata, M. and Hasegawa, T. 2013. Evaluation of the distance between Schwalbe's line and the anterior lens capsule as a parameter for the correction of ultrasound biomicroscopic values of the canine iridocorneal angle. Vet. Ophthalmo. 16, 169-174.

- Kiland, J.A., Voss, A.M., and McLellan, G.J. 2016. Effect of timolol maleat gel-forming solution on intraocular pressure, pupil diameter, and heart rate in normal and glaucomatous cats. Vet Ophthalmo. 19 (Suppl 1), 91-96.

- Kroll, M.N., Miller, P.E. and Rodan, I. 2001. Intraocular pressure measurements obtained as part of a comprehensive geriatric health examination from cats seven years of age or older. J Am Vet Med Assoc. 219, 1406-1410.

- Leibmann, J.M., Ritch, R. and Esaki, K. 1998. Ultrasound biomicroscopy. Ophtalmol Clin

297 North Am. 11, 421-433.
298 - McDonald, J.E., Kiland, J.A., Kaufman, P.L., Bentley, E., Ellinwood, N.M. and McLellan
299 G.J. 2016. Effect of topical latanoprost 0,005% on intraocular pressure and pupil diameter in
300 normal and glaucomatous cats. Vet. Ophthalmo. 19 (Suppl 1), 13-23.
301 - McLellan, G.J., Kemmerling, J.P. and Kiland, J.A. 2013. Validation of the TonoVet rebound
302 tonometer in normal and glaucomatous cats. Vet Ophthalmo. 16, 111-118.
303 - Plummer, C.E., Reigner, A. and Gellat, K. 2013. The canine glaucomas – Topical and systemic
304 medications for treatment of the glaucoma. *In*: Veterinary Ophthalmology, 5th edn. Gelatt KN,
305 Gilger BC, Kerne TJ. pp: 1104-1120.
306 - Poinsard, AS., Bastogne, T. and Balland, O. 2018. Short-term effects of ocular 2%
307 dorzolamide, 0,5% timolol or 0,005% latanoprost on the anterior segment architecture in
308 healthy cats: a prospective study. Revue Méd. Vét. 169, 203-208.
309 - Rainbow, M.E. and Dziezyc, J. 2003. Effects of twice daily application of 2% dorzolamide
310 on intraocular pressure in normal cats. Vet Ophthalmo. 6, 147-150.
311 - Rankin, A.J., Crumler, W.R. and Allbaugh, R.A. 2012. Effects of ocular administration of
312 ophthalmic 2% dorzolamide hydrochloride solution on aqueous humor flow rate and intraocular
313 pressure in clinically normal cats. Am J Vet Res. 73, 1074-1078.
314 - Sigle, K.J., Camano-Garcia, G., Carriquiry, A.L., et al. 2011. The effect of dorzolamide 2%
315 on circadian intraocular pressure in cats with primary congenital glaucoma. Vet. Ophthalmo.
316 14, 48-53.
317 - Stiles, J. 2013. Feline ophthalmology - Glaucoma. *In*: Veterinary Ophthalmology, 5th edn.
318 Gelatt KN, Gilger BC, Kerne TJ. Pp: 1514-1518.
319 - Studer, M.E., Martin, C.L. and Stiles, J. 2000. Effects of 0,005% latanoprost solution on
320 intraocular pressure in healthy dogs and cats. Am J Vet Res. 61, 1220-1224.
321 - Regnier, A., Lemagne, C., Ponchet, A., et al. 2006. Ocular effects of topical 0,03%

bimatoprost solution in normotensive feline eyes. Vet Ophthalmo. 9, 39-43.

- Wilkie, D.A. and Latimer, C.A. 1991. Effect of topical administration of timolol maleat on intraocular pressure and pupil size in cats. Am J Vet Res. 52, 436-440.

Iconography

Figure 1: Utrasound biomicroscopy (UBM) of the iridocorneal angle and ciliary cleft in a normal cat.

Figure 2: Histological aspect of the anterior segment of a dog's eye showing the main biometric parameters studied in cats.

Table I: Summary of race, age, gender and weight data for cats in the cohort.

Figure 3: Box chart of IOP variations after one week of anti-glaucoma therapy on the treated eye (DOR: dorzolamide 2%, TI: timolol 0.5%, LAN: latanoprost 0.005%).

Figure 4: Box chart of corneal thickness variations (f) after one week of anti-glaucoma treatment on the treated eye.

Table II: Mean value of the IOP (mmHg) after one week of anti-glaucoma treatment on the treated eye.

Table III: Mean value of the corneal thickness (f) (mm) after one week of anti-glaucoma treatment on the treated eye.

Table IV: Mean value of the width of the entrance of the ciliary cleft (b) (mm) after one week of anti-glaucoma treatment on the treated eye.

Table I: Summary of race, age, gender, and weight data for cats in the cohort

Group 1				Group 2				Group 3			
Breed	**Age**	**Gender**	**Weight**	**Breed**	**Age**	**Gender**	**Weight**	**Breed**	**Age**	**Gender**	**Weight**
European	5	Mn	4	European	8	Fn	5	European	1	Mn	4
European	2	Fn	4	European	1	Mn	3	European	1	Fn	3
European	8	Mn	5	European	1	Mn	3	Persian	1	M	4
European	1	Fn	4	European	6	Fn	5	European	7	Mn	5
European	1	Fn	6	European	1	Mn	3	European	6	Fn	6
Persian	2	Mn	3	European	8	Mn	6	European	9	Fn	5

European	1	F	3	Oriental shorthair	1	Mn	3	European	4	Mn	6
European	4	Mn	4	European	2	Fn	4	European	4	Mn	4
European	6	Mn	4	European	6	Fn	5	European	6	Fn	4
European	1	Mn	6	European	10	Mn	5	European	1	Mn	3
European	8	Fn	3	European	8	Fn	3	European	4	Fn	4
European	9	Mn	6	European	3	Mn	4	European	2	Mn	3
European	6	Fn	3	European	3	Fn	4	European	8	Mn	5
Somali	4	F	2	Abyssin	2	Fn	3	European	4	Mn	4
European	10	Fn	5	European	1	Fn	3	Somali	1	Fn	3

Table II: Mean value of the IOP (mmHg) after one week of anti-glaucoma treatment on the treated eye.

	Dorzolamide 2%	**Timolol 0,5%**	**Latanoprost 0,005%**
PIO Mean D0 (mmHg)	17,6	16,8	18,3
PIO Mean D7 (mmHg)	16,6	17	18,6

Table III: Mean value of the corneal thickness (f) (mm) after one week of anti-glaucoma treatment on the treated eye.

	Dorzolamide 2%	Timolol 0,5%	Latanoprost 0,005%
(f) Mean D0 (mm)	0,64	0,63	0,64
(f) Mean D7 (mm)	0,63	0,64	0,64

Table IV: Mean value of the width of the entrance of the ciliary cleft (b) (mm) after one week of anti-glaucoma treatment on the treated eye.

	Dorzolamide 2%	Timolol 0,5%	Latanoprost 0,005%
(b) Mean D0 (mm)	0,82	0,80	0,85
(b) Mean D7 (mm)	0,84	0,8	0,86